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# Health-related quality of life and behavior of triplets at adolescent age

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Abstract: OBJECTIVES: To assess health-related quality of life (HRQoL) and behavior of triplets compared with matched singletons at adolescent age and to identify medical and sociodemographic predictors of outcome. STUDY DESIGN: Fifty-four triplets (19 sets, mean [SD] gestational age 32.0 [2.4] weeks, birth weight 1580 [450] g) and 51 gestational age-, birth weight-, and sex-matched singleton controls self-rated their HRQoL at age 14.5 (0.3) years. Proxy reports about HRQoL and behavior were obtained by parents and teachers. HRQoL was measured with the Kidscreen-52 questionnaire child and parent form, and behavior with the Achenbach Child Behavior Checklist. RESULTS: Self- and parent-reported HRQoL values was similar in both groups except for the dimensions "mood and emotions" and "autonomy," which were better (P = .001, P = .03) in triplets. Parents reported significantly less behavioral problems in triplets compared with controls. Compared with community norms, both HRQoL and behavior measures in triplets were in the normal range. Parent-reported HRQoL was predicted by dichorionicity. CONCLUSIONS: HRQoL and behavioral outcome in adolescent triplets was good in our study and was, in some aspects, better than in matched singleton controls. Dichorionicity is an important outcome determinant.

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## TITLE

Health-related quality of life and behavior of triplets in adolescent age


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## KEY WORDS

Chorionicity, Socioeconomic status, Birth weight discordance, Kidscreen-52, Child Behavior Checklist, Teacher Report Form

**ABSTRACT**

**Objectives:** To assess health-related quality of life (HRQoL) and behavior of triplets compared to matched singletons at adolescent age and to identify medical and socio-demographic predictors of outcome.

**Study design:** 54 triplets (19 sets, mean (SD) gestational age 32.0 (2.4) weeks, birth weight 1580 (450) grams) and 51 gestational age-, birth weight- and gender-matched singleton controls self-rate their HRQoL at age 14.5 (.3) years. Proxy reports about HRQoL and behavior were obtained by parents and teachers. HRQoL was measured by the Kidscreen-52 questionnaire child and parent form, and behavior by the Achenbach's Child Behavior Checklist.

**Results:** Self- and parent-reported HRQoL was similar in both groups except for the dimensions 'mood and emotions' and 'autonomy', which were better (p=.001, p=.03) in triplets. Parents reported significantly less behavioral problems in triplets compared to controls. Compared to community norms, both HRQoL and behavior measures in triplets were in the normal range. Parent-reported HRQoL was predicted by dichorionicity.

**Conclusions:** HRQoL and behavioral outcome in adolescent triplets is good and in some aspects better than in matched singleton controls. Dichorionicity is an important outcome determinant.

## INTRODUCTION

In the past decades, the incidence of higher-order multiple deliveries has increased due to more frequent use of assisted reproductive technology and an increase in maternal age.[1] Triplets are at higher risk for lower cognitive functions when compared to same-gestation singletons, at least until preschool age.[2] Differences in the cognitive performance of triplets and singletons tend to attenuate at ages 5 to 7 years.[3,4] Nevertheless, knowledge about the well-being, the socio-emotional and behavioral functioning of triplets is quite scarce.[5] While we could not find any study on triplets' HRQoL, there are two longitudinal cohort studies reporting behavioral adjustment of triplets. These studies demonstrated that behavioral problems are reported for early ages (2 years), but improve thereafter.[2,3,6,7] In one study, triplets had even less behavioral problems at 7 years of age than singleton controls.[7] Factors such as mothering capacity**,** socioeconomic status (SES) and inter-triplet birth weight discordance[2, 4] are major determinants of the long-term outcome of these children. Other problems associated with multiple pregnancies and –births such as medical complications or parental stress could have independent consequences on the behavioral development and the health-related quality of life (HRQoL) of these infants and their families.[8,9] The present study aimed to investigate HRQoL and behavior in prospectively followed triplets at age 13-16 years in comparison with singletons matched for gestational age (GA), birth weight (BW) and gender. We hypothesized that triplets would generally show lower HRQoL scores and more behavior problems compared to our study reference group. We additionally examined the extent to which sociodemographic and medical characteristics are associated with HRQoL and behavior.

## METHODS

### Subjects

The cohort consists in 65 (22 sets) liveborn triplets born between July 1992 and December 1995 at the Maternity Department of the Zurich University Hospital. Triplets were recruited at birth and prospectively followed. In that period 2 other complete triplet sets were born in the Department but their parents refused to participate in the follow-up program. Triplets were matched for GA, BW and gender with singleton controls born in the same Maternity Department during the same period. All families were of Swiss origin. SES was estimated by means of a 2-to-12 points scale reflecting maternal education (range 1-6) and paternal occupation (range 1-6). Good reliability and validity of this SES-scoring system in the Swiss population has been previously demonstrated.[10]

### Procedure

The study was approved by the local research ethics committee. Written informed consent was obtained from all study subjects, their parents, and the teachers. Fifty-four triplets (19 sets) were included, as two infants died during early infancy and 3 families did not consent to participate. In the control group, 51 of the 86 contacted families fulfilling the matching criteria participated in the investigation. Controls were matched within 2 weeks of gestation, and within 700 grams birth weight, with a median difference of 1 day and 100 grams compared to triplets, respectively. Non-participants in both groups showed no significant difference compared with participants concerning GA, BW, and gender ($p > 0.4$). The Kidscreen-52 was self-completed by the adolescents while a professional person was present to help with ambiguous questions. Parents' reports and teachers' report were assessed

independently. Both mothers and fathers filled in the questionnaires on HRQoL and behavior problems together. Investigators and Teachers were aware of the triplet status of the child.

**Measures**

Before administering the HRQoL questionnaire, triplets and controls performed the Raven's Advanced Progressive Matrices.[11] This is a multiple choice intelligence test of non-verbal abstract reasoning, which provides a good measure of fluid intelligence and correlates with performance in educational domains.[11] In addition, a generic questionnaire about health condition and school situation was filled in by the subjects and their parents.

**Health related quality of life**

Self- and proxy-reported HRQoL was assessed by the Kidscreen-52. This is a generic questionnaire for children and adolescents aged between 8 to 18 years that assesses HRQoL in a multidimensional way, including physical, emotional, mental, social, and behavioural components.[12,13] The Kidscreen has been simultaneously developed in 13 European countries, including Switzerland, ensuring cross-cultural validity. The measure is available in self-report and proxy versions for parents or primary care-givers, consisting of 52 items, which are each rated on a 5-point scale.[14] The Kidscreen yields scores for ten dimensions of HRQoL. From the coded responses T-values are derived with mean of 50 and a standard deviation (SD) of 10.[12] Low T-values are indicative for poor HRQoL. The cut-off scores for subclinical and clinical are represented by a T-value ranging from 30-40 and <30, respectively. T-values and percentages are available for the German speaking Swiss population.[15]

Chronbach's Alpha values of all Kidscreen-52 dimensions of both self- and parent reports in this study ranged between 0.74 and 0.90.

**Behavior**

Subjects' parents and teachers completed the 120 and 113 respectively, problem items of the validated German version of the Child Behavior Checklist (CBCL)[16] and Teacher Report Form (TRF).[17] These are standardized proxy-report measures of behavioral problems of children and adolescents between 4 and 18 years with excellent psychometric properties.[16,17] Raw scores are coded for 3 composite global scales (total problems scale, externalizing and internalizing global problem scale) and 8 behavior subscales. Results are presented as T-values (population mean=50, SD=10) with higher scores indicating more severe behavior problems. The cut-off scores for subclinical and clinical cases in the syndrome scales range from 65-69 and >69, respectively, whereas for the global scales subclinical and clinical T-values are defined as a 60-63 and >63, respectively.[16,17] In this study, Cronbach's Alphas values ranged between 0.86 and 0.93 for the 3 global behavior scales of both CBCL and TRF**.**

**Statistics**

Statistical analyses were performed with SPSS 18.0 (SPSS Inc., Chicago, USA) as followed: independent t-test to compare normally distributed groups' variables and to compare the HRQoL and Behavior measures; Mann-Whitney U-test and $X^2$ test to compare not normally distributed variables and frequencies in the two groups, respectively; one-sample t-test to compare results with norm references and effect sizes were evaluated based on established conventions.[18] When analyzing predictors

for adverse outcome, triplets were regarded as sets based on the statistical assumption that they are not fully independent individuals. The total self- and parents' rated HRQoL score and the main CBCL/TRF scales were the dependent variables. Linear mixed models were applied (S-Plus 8.0 for Windows, Insightful Corporation) using the 'lme' function.[19] Grouping and random factors were the triplet status and the intercept, respectively, which makes the analysis equivalent to a Repeated Measure ANOVA. In a first step, potential outcome predictors were included in the model equation one at a time. In a second step, multiple regression analysis was performed to evaluate the independent effect of predictors on the main outcome measures. Predictors were selected on the basis of results of previous studies and based on the statistical significance in the univariate analyses.

## RESULTS

### Study population

Perinatal and outcome variables for triplets and controls are presented in Table I. Except for a higher rate of cesarean section and of assisted reproduction mode in triplets no other significant differences in perinatal variables were found between the groups. No surviving triplet was from a monochorionic placenta. Two triplet pregnancies presented with a dichorionic and diamniotic placenta and 8 triplets were monozygotic. Sociodemographic characteristics, cognitive abilities and therapies were similar between the two groups except for a higher rate of single parent household and a lower number of siblings living in the same home in the controls compared with the triplets. Within triplets and controls, SES, single-parent household, and the number of siblings were not correlated (Spearman's range $r = .01 – .17$, $p = .22 – .96$).

**Health-related quality of life**

Means and SDs of the Kidscreen-52 dimensions are listed in Table II. We observed no significant differences in all dimensions of self-reported HRQoL between triplets and controls. Parent-reported HRQoL was higher in triplets than in controls in 2 domains: ‘moods and emotion’ and ‘autonomy’. After correction for SES, single parent household and number of siblings, triplets had higher self-reported ‘autonomy’ and parent-reported ‘moods and emotion’ dimensions than controls. Comparison of child and parent reports revealed that parents of triplets reported poorer HRQoL for their offspring than the triplets themselves. However, differences reached statistical significance only in the dimensions ‘psychological well-being’ (p=.004) and ‘autonomy’ (p=.02) (data not shown). Self-reported HRQoL of triplets was significantly higher in the majority of dimensions (7/10) compared to Swiss norms. Parent-reported HRQoL revealed higher mean values for triplets compared with Swiss norms in the dimension ‘moods and emotions’.

**Behavior**

Means and SDs of the CBCL and the TRF are presented in Table III. Parents reported significantly less behavioral problems in the triplets compared to singleton controls for all main CBCL scales. TRF scores of triplets were significantly lower in the ‘internalizing global problem scale’ than controls. Only scores of the ‘internalizing global problem scale’ of the TRF in triplets remained significantly lower than in controls after correction for SES, single parent household, and number of siblings. Comparing the main scales of CBCL- and TRF-values of triplets with those of the

normative test-references revealed that triplets had significantly lower scores for the total- and externalizing global behavior problem scale.

**Predictors of HRQoL and behavior of triplets**

Table IV summarizes the linear mixed models predicting self- and parent-reported HRQoL as well as parent- and teacher-reported behavior of triplets. In the univariate analysis dichorionicity was associated with lower self- (p=.01) and parent-reported (p<.001) HRQoL, lower SES with lower self-reported HRQoL (p=.03) and male gender with the higher scores in the 'total behavior problem scale' of the CBCL (p = .03). However, caesarean section, mode of conception and perinatal complications were not associated with HRQoL and behavior (Table X; online). In the multivariate analysis dichorionicity was found to be the only significant predictor of parent-reported HRQoL.

**DISCUSSION**

This study is the first to examine self- and proxy-rated HRQoL and behavior problems in a cohort of triplets at adolescent age in comparison to GA-, BW- and gender-matched singletons. The results contradict our initial hypothesis: self-reported HRQoL was similar in triplets and singleton controls, whereas triplets had less behavioral problems compared with singleton controls. Further, compared to test norms, triplet's HRQoL and behavior were in the normal range. Dichorionicity was a significant predictor for poorer HRQoL.

Our results are in line with studies reporting on low and extremely low BW singleton teenagers who do not perceive their self-reported HRQoL differently than their term peers.[20, 21] It has been found in singletons that prematurity affects HRQoL

at all age periods, however, the impact is highest in early life, extends to young adulthood, but seems to diminish over time.[22] This might support our results of a normal HRQoL in adolescent triplets.

With regard to the self-reported 'autonomy' and parent-reported 'emotional' and 'school environment' dimensions, triplets rated these dimensions better than singletons controls. Triplets might have benefited from the higher number of siblings and have become more competent with emotional stress situations. Sibling relationships may be characterized as companionate behavior and empathy, which can be related to more favorable outcomes.[23] In addition, triplets possibly learn more rapidly and effectively to manage family and general responsibilities compared with singletons. A faster autonomy development in triplets could also be the consequence of the lower parent-infant synchrony, as well as less distress during maternal separation and less approach at reunion to parent, which have been observed in triplets yet at age 2 years.[24]

The fact that parents perceive their offspring's HRQoL slightly poorer than the children themselves, irrespective of triplet or control status, reflects the different perspectives in the parent-child dyad, which has also been reported for other groups.[20,21]

Our results on the behavioral outcome of triplets are supported by previous longitudinal studies showing equal[3] or less[7] behavioral problems in triplets. Triplets in those studies were younger (5 and 7 years), but a catch-up trend with an attenuation of developmental problems over time was noted. That is otherwise observed in the cognitive development in triplets.[3,4] Although it is not clearly known if the number of siblings affects behavioral development of children, it has been shown that sibling relationships, SES, and family structure, as well as number of parents in the

household, affect child adjustment health.[25] In our study, differences between the behavioral outcome of the two groups were in part redimensioned after adjustment for some of these socio-demographic factors and an association between higher rate of single parent household status in the control group and the global CBCL scales was observed (data not shown). In addition, although there was no significant difference in the SES between triplets and controls, triplets families tended to have a higher SES.

It seems that immaturity at birth strongly correlated with attention problems, autism spectrum disorders and internalizing symptoms.[26] This has been also shown in late-preterm.[27] These findings are not in agreement with our results. A possible interpretation concerning this positive behavioral outcome is given by the setting of our study. As our cohort of triplets has been followed longitudinally from birth on as a potential high-risk population, health and education practitioners may have been sensitized to behavior problems and thus introducing interventions earlier. This could have also positively affected HRQoL, which in our sample was rated very high both by parents and triplets themselves. Triplet populations that are not managed in such a comprehensive way might show a poorer outcome.

One significant predictor for lower HRQoL but no significant predictors for behavioral maladjustment could be identified in this study. Despite the small number of subjects, dichorionicity, i.e. one placenta shared by 2 of 3 triplets, had the largest effect on triplets' outcome. This is in line with previous studies showing that chorionicity is associated with a higher risk of developing neurodevelopmental deficits in later life.[28] SES, which is a construct most widely associated with health, cognitive, and socioemotional outcomes in children[10,29] was not independently associated with our outcome measures. This is probably caused by the statistical

approach, which considered the sets of triplets as dependent, thus further reducing the sample size. The same could be hypothesized for the lacking influence of gestational age.

We expected that birth weight discordance would affect HRQoL or behavior of triplets, according to its negative influence on cognitive and motor outcome of triplets.[2,4] This association was not observed in this sample however, may be because of the low number of discordant triplets. On the other hand it is possible that the influence of weight discordance decreases with increasing age.

Three principal strengths of this study are: a) the comparison of triplets with a control group of matched singletons; b) the multidimensional and multiinformant character of the outcome data on the subjects' HRQoL and behavior; and c) the availability of Swiss norms for our HRQoL measure.

The main limitation of the present work is the rather small sample size, which is a frequent weakness in triplets' studies.[2,3,6,7,9] Other limitations concern the teachers' reports. The response rate of teachers was relatively low, and their selection and awareness of the triplet status of the index subjects could have resulted in a source of bias. Finally, a selection bias in the recruitment of the controls could have occurred, as a number of contacted families refused to participate and as families with a higher proportion of single mothers and with a lower number of siblings was recruited compared to the triplets' families.

In conclusion, the results of this study indicate that HRQoL and behavioral outcome in adolescent triplets is good and in some aspects even better than in matched singleton controls. Dichorionicity plays a major role in the prediction of long-term outcome of these children. The results of our work allow identifying triplets at particular risk for poorer quality of life and behavioral problems. Furthermore, our

results provide a basis for better parental counseling in regard to long-term outcome of their triplets and implementation of early interventions.

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**ABBREVIATIONS**

| | |
|---|---|
| HRQoL | Health-related quality of life |
| SES | Socioeconomic status |
| GA | Gestational age |
| BW | Birth weight |
| SD | Standard deviation |
| CBCL | Child Behavior Checklist |
| TRF | Teacher report form |

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